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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,642	10/11/2001	Jonathan M. Cohen	112163.124 U	1956

7590 05/18/2005
Hale & Dorr
1455 Pennsylvania Avenue N W
Washington, DC 20004-1008

EXAMINER

YANG, NELSON C

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 05/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/856,642

Applicant(s)

COHEN, JONATHAN M.

Examiner

Nelson Yang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 February 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3,5-8,11-19 and 21-29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3,5-8,11-19 and 21-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>4/30/04</u> . | 6) <input checked="" type="checkbox"/> Other: <u>IDS: 2/18/05</u> . |

PD

DETAILED ACTION

Response to Amendment

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 18, 2005 has been entered.
2. Applicant's amendment of claims 17, 21-23 is acknowledged and has been entered.
3. Applicant's addition of claims 24-29 and cancellation of claim 20 are acknowledged and have been entered.
4. Claims 3, 5-8, 11, 12, 14-19, 21-29 are currently pending.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
6. Claims 3, 5-8, 11, 12, 14-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
7. Claims 21-29 recite producing a stain by a multi-step staining process, but fails to establish what these steps are, rendering it unclear how one of ordinary skill in the art would perform this multi-step staining process, or what would be required in these steps.

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In particular, it is unclear how the production of the stain differs from the application of the stain. In applicant's arguments, applicants state that the steps include pretreatment of the tissue, antibody treatment, secondary antibody treatment, substrate reaction, counterstaining, and the like, which would appear to be steps involved in applying the stain to the tissue samples.

8. The remaining claims are indefinite due to their dependence on an indefinite claim.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 3, 5-8, 11, 12, 17-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kononen et al [Kononen et al, Tissue microarrays for high-throughput molecular profiling of tumor specimens, Nature Med. July 1998, 4(7), 844-847] in view of Kalra [US 5,948,359].

With respect to claims 3, 5-7, 20-23, Kononen et al teach providing a plurality of tissue microarrays (p.844, cols. 1-2), providing DNA, RNA or protein targets in each of the tissue samples in the arrays (p.844, col.1), providing and applying stains to that bind to the target molecule in situ to the tissue microarrays (p.847, col.1), and correlating extent of stain binding with clinical utility of the target molecule, such as markers for determining the presence of tumours (p.847, col.1), in order to establish the diagnostic, prognostic and therapeutic importance of emerging cancer gene candidates (abstract). Although Kononen et al teach the use of automation to permit simultaneous construction of multiple tumor array blocks and further

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teach that doing so would allow the creation of dozens of replicas of tumor arrays, each providing up to 200 sections for molecular analysis (p.845, col.2), each section containing as much as 1000 tissue samples (p.846, col.2). Kononen et al do not specifically disclose that the application of the stains of the tumor arrays is automated in a high throughput manner.

It would have been obvious, however, to one having ordinary skill in the art at the time the invention was made to automate the staining, since it has been held that broadly providing a mechanical or automatic means to replace manual activity which has accomplished the same result involves only routine skill in the art. In re Venner, 120 USPQ 192. Furthermore, Kalra et al teach that modern laboratories find it desirable to automate the staining process in order to examine large numbers of tissue specimens (column 1, lines 16-31), while Kononen et al teach that large number of tumor arrays with identical sample coordinates would allow for parallel detection of DNA, RNA, or protein targets, allowing for consecutive analyses of a large number of molecular markers and construction of a database of correlated genotypic or phenotypic characteristics of uncultured human tumors (p.844, col.1-2).

Therefore it would be obvious to use an automated stainer to apply the stain to the tissue samples in a high-throughput manner in the method disclosed by Kononen et al, as suggested by both Kononen et al and Kalra et al, in order to examine large numbers of tissue specimens, which would allow for parallel detection of DNA, RNA, or protein targets, allowing for consecutive analyses of a large number of molecular markers and construction of a database of correlated genotypic or phenotypic characteristics of uncultured human tumors.

11. With respect to claims 8, 11, 12, Kononen et al teach that the use of DNA, RNA, or protein targets in each of hundreds of tissue specimens in an array (p.844, col.1).

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12. With respect to claim 17-19, Kononen et al teach a tissue microarray that has a solid surface with tissue samples mounted to the solid surface (p.844, column 1). Kononen et al do not teach the use of a bar code labeled slide for identifying how the tissues are to be treated by a machine.

Kalra et al, however, does teach the use of slides with bar code labels for optional features that can be included on the apparatus include devices intended to ensure level operation, to protect against electric shock, to verify that an appropriate tip has been selected and properly placed on the tip head, or to optically scan slides in a microscope slide tray or other container for microscope slides so that a user is not required to enter information into the computer (column 20, lines 1-15).

Therefore, it would be obvious to use slides with bar-code labels in the method of Kononen et al, as suggested by Kalra et al, so that a user is not required to enter information into the computer.

13. Claims 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kononen et al [Kononen et al, Tissue microarrays for high-throughput molecular profiling of tumor specimens, Nature Med. July 1998, 4(7), 844-847], in view of Kalra et al [US 5,948,359] as applied to claims 1-13, 17-20 above, and further in view of Bogen et al [US 6,183,693].

With respect to claims 14, Kalra et al teach the use of an automated stainer capable of heating (column 6, lines 4-19), but do not teach that the automated stainer comprises a first heater and a second heater and is capable of heating slides at different temperatures.

Bogen, however, teaches that since various staining procedures require heat at different times to enhance the rate of chemical reaction, a means has been developed to heat slides to different temperatures, independently of the temperatures of other slides (column 1, line 60-column 2, line 5). Specifically, Bogen teaches a plurality of flat heating stations are provided on the platform, each heating station supporting at least one microscope slide and, in a preferred embodiment, each heating surface supporting a single microscope slide. The heating stations are individually controlled to control temperatures to which the slides are heated (column 2, lines 33-44), since various procedures require heat at different times to enhance the rate of chemical reaction (column 1, line 60-column 2, line 5).

Therefore it would be obvious to use an instrument with multiple heaters in the method of Kononen et al and Kalra et al, as taught by Bogen et al, in order to enhance the rate of chemical reaction during staining.

14. With respect to claims 15 and 16, Bogen et al teach a carousel adapted to support a plurality of microscope slides bearing biological samples. A plurality of flat heating stations are provided on the platform, each heating station supporting at least one microscope slide and, in a preferred embodiment, each heating surface supporting a single microscope slide. The heating stations are individually controlled to control temperatures to which the slides are heated (column 2, lines 33-44), since various procedures require heat at different times to enhance the rate of chemical reaction (column 1, line 60-column 2, line 5).

Therefore, it would be obvious to include multiple heaters mounted on a carousel with means for monitoring and controlling the temperature of the heaters, as taught by Bogen, in the

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apparatus of Kalra et al and Kononen et al, in order to enhance the rate of the chemical reaction during staining.

Response to Arguments

15. Applicant's arguments filed February 18, 2005 have been fully considered but they are not persuasive.

16. With respect to applicant's arguments that stains that bind to the target molecule(s) are produced by a multi-step staining process, this is not found persuasive. While it is acknowledged that *in situ* hybridization and immunohistochemical staining are multi-step staining processes, Kononen et al do teach producing stainins such as immunohistochemistry and *in situ* hybridization (p.847, col.1).

17. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the steps recited by applicant on p.11 such as pretreatment of the tissue, retrieval of antigens, rinsing, etc.) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

It should also be noted, the recitations of performing immunohistochemistry and *in situ* hybridization have not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural

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limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

18. In response to applicant's arguments against the references individually on pgs.12-13, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In particular, while it is true that Kalra et al only teaches staining up to 40 single tissue slides at a time, Kononen et al teaches the production of tissue slides with up to 1000 tissue samples (p.846, col.2). Therefore, by staining the slides of Kononen et al, the automated stainer of Kononen could stain up to 40,000 tissue samples.

19. The remainder of the arguments appear to refer to the arguments that claims 21-23 are allowable. Since the arguments with respect to claims 21-23 were not found persuasive, applicants arguments with respect to claims 8, 11, 12, and 14-19 are not found persuasive.

Conclusion

20. No claims are allowed.


21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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22. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nelson Yang
Patent Examiner
Art Unit 1641


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05/16/05